

### **REMARKS/ARGUMENTS**

Claims 1-16, 19-48 and 50-65 were pending in the present application before this Amendment as set forth above. By the Amendment, claims 1, 33, 46, and 60 are amended and claims 15, 61-63, and 45 are canceled without prejudice.

In the Non-Final Office Action mailed June 15, 2010 (hereinafter “the Office Action”), claims 1-5, 8-16, 19-22, 33-38, 41-48 and 50-65 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Pub. No. 2003/0003571 to Kanegasaki et al. (hereinafter “Kanegasaki”), in view of U.S. Patent No. 5,520,787 to Hanagan et al. (hereinafter “Hanagan”) and U.S. Patent No. 5,589,352 to Breznak et al. (hereinafter “Breznak”). In addition, claims 25-32 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, Hanagan, and Breznak, and further in view of U.S. Patent Pub. No. 2004/0142409 to Allen et al. (hereinafter “Allen”). Also, claims 6, 7, 39 and 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, Hanagan, and Breznak, and further in view of U.S. Patent Pub. No. 2006/0194273 to Thomas (hereinafter “Thomas”).

Applicant very much appreciates the Examiner’s careful review of the instant application.

In response, as set forth above, claims 1, 33, 46, and 60 have been amended for better form. For example, features of originally filed claims 15, 45, and 62, now canceled, have been incorporated into amended claims 1, 33, and 60, respectively. In addition, without acquiescing to the propriety of the Examiner’s rejections and to facilitate prosecution of the instant application, claims 15, 45, and 61-63 have been canceled without prejudice, which renders the Examiner’s rejections under 35 U.S.C. § 103 moot. Applicant reserves every right in these canceled claims to file continuation applications.

Support for the amendments can be found in the disclosure as originally filed, for example in the claims as originally filed, in paragraphs on page 18, lines 16-24 and page 20, lines 26-38 to page 27, lines 1-34 of the specification, and in Figs. 1A, 1B, and 2 of the drawings. Applicant submits that no new matter has been added.

Any amendments to the claims not specifically referred to herein as being included for the purpose of distinguishing the claims from cited references are included for the purpose of clarification, consistence and/or grammatical correction only.

It is now believed that the application is in condition for allowance at least for the reasons

set forth below and such allowance is respectfully requested.

The following remarks herein are considered to be responsive thereto.

***Rejections under 35 U.S.C. § 103 over Kanegasaki, Hanagan, and Breznak***

In the Office Action, claims 1-5, 8-16, 19-22, 33-38, 41-48 and 50-65 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hanagan. Applicant respectfully traverses these rejections for at least the reasons set forth below.

**Claims 1-14, 16, and 19-32:**

As set forth above, amended ***claim 1*** recites “a bioreactor for cultivating living cells in a liquid medium comprising: a first substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving and culturing the cells and receiving the liquid medium; ***a barrier*** dividing the chamber into a first subchamber and a second subchamber, wherein the barrier has ***a porosity*** to allow the first subchamber and the second subchamber to be in fluid communication and allow at least one predetermined type of cells ***to permeate*** between the first subchamber and the second subchamber; a second substrate positioned adjacent to the first surface of the first substrate; a third substrate, wherein the third substrate is positioned adjacent to the second surface of the first substrate; and an electrochemical measuring system positioned in the third substrate and adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber, ***wherein the barrier comprises a porous material.***” (Emphasis added.)

In one exemplary embodiment of the present invention as shown in Figs. 1A and 1B of the drawings as originally filed, a bioreactor 100 includes a first substrate 140 having a first surface 140a and an opposite second surface 104b, defining a chamber 101 therebetween for receiving cells and a liquid medium. As described in the specification as originally filed, the bioreactor 100 “has ***a barrier 104*** dividing the chamber 101 into a first subchamber 102 and a second subchamber 103, wherein the barrier 104 has ***a porosity*** to allow the first subchamber 102 and the second subchamber to be in fluid communication and allow at least one predetermined type of cells ***to permeate*** between the first subchamber 102 and the second subchamber 103.” (Page 20, lines 26-35.) (Emphasis added) In one embodiment, ***the barrier 104 comprises a***

*porous material* and may include a nanofilter (see page 18, lines 16-24 and page 22, lines 27-35 of the specification as originally filed.)

In contrast, as understood by Applicant, Kanegasaki discloses “a well unit to be used in an apparatus whereby movements of cells based on their own actions can be accurately and easily detected, in case of detecting the chemotaxis of cells due to a chemotactic factor or the inhibition of the chemotaxis of cells by an inhibitor.” (Kanegasaki, [00090].) In Kanegasaki, *grooves or terraces*, for example, grooves 5 on a bank 10 in a channel 1 (see, e.g. Figs. 2, 4 and 6) are used for controlling position-adjustment of cells in the wells. (See also Kanegasaki, [0097].) The grooves have *a width and/or a depth* configured according to the *diameter or deformability of cells provided*. (Kanegasaki, [0084].) In other words, Kanegasaki does not disclose, teach, or even remotely suggest *a barrier comprising a porous material wherein the porosity of the barrier allows for one or more predetermined types of cells to permeate between a first subchamber and second subchamber*.

Kanegasaki does not disclose, teach, or suggest “[a] bioreactor for cultivating living cells in a liquid medium comprising: a first substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving and culturing the cells and receiving the liquid medium; *a barrier* dividing the chamber into a first subchamber and a second subchamber, wherein the barrier has *a porosity* to allow the first subchamber and the second subchamber in fluid communication and allow at least one predetermined type of cells *to permeate* between the first subchamber and the second subchamber; a second substrate positioned adjacent to the first surface of the first substrate; a third substrate, wherein the third substrate is positioned adjacent to the second surface of the first substrate; and an electrochemical measuring system positioned in the third substrate and adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber, *wherein the barrier comprises a porous material*”, as recited in amended claim 1. (Emphasis added.) Therefore, Kanegasaki does not disclose, teach, or suggest a bioreactor having all of the features recited in amended claim 1.

The Examiner attempts to cure the deficiencies of Kanegasaki with the disclosures of Hanagan and Breznak. Hanagan, as understood by Applicant, discloses “a diagnostic flow cell for determining the presence or amount of an analyte in a test sample...[comprising] (i) a

spacing layer disposed between a first and a second opposed substrate, wherein the spacing layer has a longitudinal void and wherein the spacing layer and opposed substrates define a flow channel; (ii) fastening means for coupling the spacing layer and the opposed substrates; (iii) inlet means for permitting a sample to enter the flow channel; (iv) outlet means for permitting the sample to exit the flow channel; and (v) immobilized reagent means for producing a detectible signal, wherein the reagent means is at least partially contained within the flow channel.”

(Hanagan, Col. 1, lines 54-66.) Hanagan does not disclose, teach, or suggest a bioreactor having all of the features recited in amended claim 1, taken alone or in combination with Kanegasaki. Breznak, as understood by Applicant, discloses a system and method for “observation of microorganisms in a controlled environment” using a diffusion gradient chamber with reservoirs. (Breznak, Abstract.) Breznak does not disclose, teach, or suggest a bioreactor having all of the features recited in amended claim 1, taken alone or in combination with Kanegasaki and/or Hanagan. Therefore, none of Kanegasaki, Hanagan, and/or Breznak, taken alone or in combination, disclose, teach, or suggest a bioreactor having all of the features recited in amended claim 1.

For at least the reasons set forth above, Applicant respectfully submits that the Examiner has failed to make a *prima facie* case to support the rejection of claim 1 under 35 U.S.C. §103(a) over Kanegasaki, Hanagan, and/or Breznak. First, there is no suggestion or motivation to modify the references or combine the reference teachings. Second, there is no reasonable expectation of success of combining the reference teachings. Finally, the combination of references does not teach or suggest all elements of Applicant’s claims.

In supporting the obviousness rejections under 35 U.S.C. §103, the Examiner “bears *the initial burden...of presenting a prima facie case of unpatentability*...After evidence or argument is submitted by the applicant in response, patentability is determined *on the totality of the record*.” *Ex parte Wada and Murphy*, BPAI Appeal No. 2007-3733 (January 14, 2008), and “*Office personnel must articulate*”, among other things, “*a finding that the prior art included each element claimed ...*”, MPEP 2143 (A)(1). The “*unwitting application of hindsight*” is *inappropriate*. *Ex parte So and Thomas*, BPAI Appeal No. 2007-3967 (January 4, 2008). In other words, the Examiner’s “rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational

underpinning to support the legal conclusion of obviousness.” *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). (MPEP § 2142). (Emphasis added.)

For at least the foregoing reasons, Applicant respectfully submits that claim 1, as amended, is patentable under 35 U.S.C. § 103(a) over any combination of Kanegasaki, Hanagan, and/or Breznak.

Accordingly, claims 2-14, 16, and 19-32, which depend from now allowable amended claim 1, are also patentable for at least this reason.

**Claims 33-44, 46-48, and 50-59:**

As set forth above, amended ***claim 33*** recites “[a] bioreactor for cultivating living cells in a liquid medium comprising: a substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving and culturing the cells and receiving the liquid medium, wherein the chamber is formed with a center and a boundary; ***a first barrier*** enclosing the center and a portion of the chamber to form a central chamber; ***a second barrier*** positioned between the first barrier and the boundary so as to form an intermediate chamber and an outer chamber; and means for electrochemical measurements of the cells responsive to the liquid medium in at least one of the outer chamber, the intermediate chamber and the central chamber, wherein ***the first barrier has a first porosity*** to allow the central chamber and the intermediate chamber to be in fluid communication and allow at least a first predetermined type of cells ***to permeate*** between the central chamber and the intermediate chamber, ***the second barrier has a second porosity*** to allow the outer chamber and the intermediate chamber to be in fluid communication and allow at least a second predetermined type of cells ***to permeate*** between the outer chamber and the intermediate chamber, ***and wherein the first barrier comprises a porous material.***” (Emphasis added.)

In one exemplary embodiment of the present invention as shown in Fig. 2 of the drawings of the disclosure as originally filed, a bioreactor 700 includes a substrate 730 having a first surface and an opposite second surface, defining a chamber 732 therebetween for receiving cells and a liquid medium, wherein the chamber 732 is formed with a center 734 and a boundary 736. The bioreactor 700 also has ***a first barrier 738***, which encloses the center 734 and a portion of the chamber 732 to form a central chamber 706, and ***a second barrier 740***, which is positioned

between the first barrier 738 and the boundary 736 so as to form an intermediate chamber 705 and an outer chamber 704. As described in the specification as originally filed, “***the first barrier 738 has a first porosity*** to allow the central chamber 706 and the intermediate chamber 705 [to be in] fluid communication and allow at least a first predetermined type of cells ***to permeate*** between the central chamber 706 and the intermediate chamber 705, and ***the second barrier 740 has a second porosity*** to allow the outer chamber 704 and the intermediate chamber 705 [to be] in fluid communication and allow at least a second predetermined type of cells to permeate between the outer chamber 704 and the intermediate chamber 705.” (Page 24, lines 23-38.) (Emphasis added.) In one embodiment, ***the first barrier 738 is formed with a porous material*** (see, e.g., page 25, lines 35-38 to page 26, lines 1-13 of the specification as originally filed).

Incorporating herewith the reasons set forth above why amended claim 1 is patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak, Applicant respectfully submits that amended claim 33 is also patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak for at least these reasons.

Accordingly, claims 34-44, 46-48, and 50-59, which depend from now allowable independent claim 33, are also patentable for at least this reason.

**Claims 60, 64, and 65:**

As set forth above, amended ***claim 60*** recites “[a] bioreactor for cultivating living cells in a liquid medium comprising: a substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving and culturing the cells, and receiving the liquid medium with a boundary; and ***means for dividing the chamber into plurality of chambers***; and means for electrochemical measurements of the cells responsive to the liquid medium in at least one of the plurality of chambers, wherein each of the plurality of subchambers is in fluid communication with at least another one of the plurality of subchambers, ***wherein the dividing means comprises a barrier*** to divide the chamber into a first subchamber and a second subchamber, wherein the barrier has ***a porosity*** to allow the first subchamber and the second subchamber to be in fluid communication and to allow at least one predetermined type of cells ***to permeate*** between the first subchamber and the second subchamber, and ***wherein the barrier comprises a porous material***.” (Emphasis added.)

Incorporating herewith the reasons set forth above why amended claim 1 is patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak, Applicant respectfully submits that amended claim 60 is also patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak for at least these reasons.

Accordingly, claims 64 and 65, which depend from now allowable amended claim 60, are also patentable for at least this reason.

***Rejections under 35 U.S.C. § 103 over Kanegasaki, Hanagan, Breznak, and Allen***

In the Office Action, claims 25-32 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, Hanagan, and Breznak, and further in view of Allen. Applicant respectfully traverses the rejections. Applicant respectfully submits that ***Allen is not a qualified reference*** because Allen claims a priority date of October 21, 2002 from U.S. provisional patent application number 60/420,078, which is later than August 27, 2002, the filing date of U.S. provisional patent application number 60/406,278, to which the present application claims priority. Thus, claims 25-32 are submitted to contain patentable subject matter in their own merits. Moreover, even assuming that Allen were a qualified reference, which Applicant submits that it is not, as set forth above claims 25-32 depend from now allowable amended claim 1 and are therefore patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Allen for at least this reason.

***Applicant notes that the remarks set forth above regarding claims 25-32 were also presented in Applicant's Amendment dated April 5, 2010.*** However, as understood by Applicant, the Examiner did not fully consider these remarks and/or provide any response thereto in this Office Action. Accordingly, ***Applicant respectfully requests that the remarks set forth above be considered and that any claim rejections using the Allen reference be withdrawn.***

***Rejections under 35 U.S.C. § 103 over Kanegasaki, Hanagan, Breznak, and Thomas***

In the Office Action, claims 6, 7, 39, and 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, Hanagan, and Breznak, and further in view of Thomas. However, these rejections are moot in light of amendments to now allowable independent claims 1 and 33. As set forth above, claims 6 and 7 depend from now allowable amended claim 1, and

claims 39 and 40 depend from now allowable amended claim 33. Accordingly, claims 6, 7, 39, and 40 are also patentable for at least this reason.

Further, even assuming that these rejections were not rendered moot for the reasons set forth above, Applicant respectfully submits that claims 6, 7, 39 and 40 are allowable over any combination of Kanegasaki, Hanagan, Breznak, and/or Thomas for at least the additional reason that Thomas fails to cure the deficiencies of Kanegasaki, Hanagan, and Breznak. As understood by Applicant, Thomas discloses an apparatus and methods for cell-based assays. (see, e.g. Thomas, [0002].) Thomas does not disclose, teach, or suggest a bioreactor having all of the features recited in claims 6, 7, 39 and 40, taken alone or in combination with the features recited in now allowable amended independent claims 1 and 33. Accordingly, individual consideration and allowance of each claim is respectfully requested.



### **CONCLUSION**

Applicant respectfully submits that the foregoing Response places this application in condition for allowance. If the Examiner believes that there are any issues that can be resolved by a telephone conference, or that there are any informalities that can be corrected by an Examiner's amendment, to facilitate the prosecution, please call the undersigned at 404.495.3678. No fee is due, but the Commissioner is hereby authorized to charge any petition fee under 37 CFR 1.17(f),(g) or (h) or any deficiency of fees and credit of any overpayments to Deposit Account No. 50-3537.

Respectfully submitted,

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